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Commentary

Positron emission tomography as a tool to study human vision and attention

Maurizio Corbetta

Department of Neurology and Neurological Surgery, Washington University, St. Louis, MO 63110

Introduction and Rationale for Positron Emission Tomography (PET) Activation Studies

The study of vision is probably the most advanced in systems neuroscience. Significant progress has been made over the last 30 years in understanding the anatomical, physiological, and computational organization of the visual system in the primate brain (1). Since the seminal work of David Marr (2), a major goal in vision research has been to characterize vision as a complex computational task and the visual system as an information-processing device. From this systems perspective, it is becoming more evident that the elementary processing components within the visual system are not isolated neurons, but neuronal assemblies within cortical or subcortical areas. The visual system (and brain systems in general) has been characterized as a distributed multilevel hierarchy of visual areas in which both serial and parallel processing occur simultaneously.

Single neuron recordings in awake-behaving monkeys has been a powerful way to correlate neuronal activity and visual behavior. The above considerations suggest, however, that a more complete understanding of visual processing requires the analysis of neuronal activity from a wider spatial window. This analysis is now being provided by several techniques, such as 2-deoxyglucose autoradiography and optical imaging in primates and neuroimaging [PET and functional magnetic resonance imaging (fMRI)] methods in humans.

The basic rationale for using PET to study human visual neurophysiology is that the performance of any task places specific information processing demands on the brain. These demands are met through changes in neural activity in various functional areas of the brain. Changes in neuronal activity produce changes in local blood flow (3, 4), and these variations in blood flow can be measured with PET.

It is currently believed that changes in blood flow correspond to changes in neuronal activity at the level of one or a few adjacent cortical or subcortical functional areas. The spatial localization of the method—i.e., the accuracy of localizing a single source—is ≈2–5 mm (see, e.g., ref. 5), in the order of magnitude of most brain areas. The temporal resolution of a PET activation study, when using a short-lived tracer such as ^{15}O-labeled water (half-life ≈ 2 min), is about 40 sec. A major drawback of the poor temporal resolution is the inability to discern the temporal relationships among multiple regions of activation. Furthermore, only processes that are repeated many times over the 40 sec can be imaged through appropriate experimental designs. It is possible that partial resolution of some of these issues will be provided by coupling PET recording with faster methods (magnetoencephalography, evoked response potentials, electrocorticography).

In summary, PET allows monitoring of brain neural activity that has been averaged over time at the level of individual functional areas. PET spatio-temporal performance characteristics better suit experimental designs that look at the activation of distributed networks in the brain rather than at the fine mapping (e.g., retinotopical organization) of cortical areas in space or time.

Studies of Vision and Attention

PET-imaging studies of visual functions have used two different kinds of experimental strategy. One strategy, which might be called "bottom-up," manipulates the visual input presented to a subject to assess the attributes of a stimulus processed by the area or areas under study. Another strategy, which might be called "top-down," varies the kind of processing or task demands and holds the visual input constant. Critical to this second approach is a clear definition of the processing components to be imaged, and the development of psychophysical tasks where those components can be reliably measured in terms of performance.

The study of Dupont *et al.* (6) in this issue represents an excellent example of this top-down approach with PET. In all scans, subjects viewed the same set of oriented stationary gratings. In different conditions, subjects either maintained fixation on the display (passive task), detected its onset (detection), identified its orientation (identification), or discriminated the orientation of two stimuli that were sequentially presented in a delayed match-to-sample task (same trial discrimination, STD). The same visual input was therefore processed by the visual system under conditions that progressively tapped different and computationally more demanding visual processes. Several areas in occipital cortex were more active in the active conditions (detection, identification, STD) than in the passive condition. More importantly, a region in right occipital cortex (nearby area 19 of Brodmann) remained selectively activated when the identification task was subtracted from the STD task. The authors argue that this subtraction specifically isolates short-term memory and matching operations for orientation that were unique to the STD task, by equating other processes such as low-level analysis, fine discrimination, and focused attention.

These results have several implications for studies of vision and attention in the human visual system.

First, they provide support to the idea of functional specialization in the human visual system, in line with anatomophysiological evidence from the animal literature—in particular, primate neurophysiology. The activation for orientation in the right superior occipital gyrus of Dupont *et al.* (6), which has been recently replicated in another study from the same group (7), is at a different location from other extrastriate regions activated by different sets of stimuli. For instance, random arrays of moving dots have consistently activated in different laboratories a region at the temporo–occipital–parietal junction, which is thought to be analogous to the motion-specific area MT or V5 in monkey (8). Another region in the ventromedial portion of the occipital lobe, in the lingual and/or fusiform gyrus, has been activated by isoluminant color stimuli and color discrimination (8–10). It has been proposed that this region might be the human analogue of area V4 in monkey. At this time these analogies are tentative, but intriguing. They are based on (*i*) the specificity of the re-

sponse to carefully selected visual stimuli that are used to drive these regions in PET and single-unit recording and on (*ii*) the similarity across species of the underlying psychophysical deficit after their destruction (11–14). Several other regions have been activated in extrastriate cortex during processing of shape (10, 15), dot location (16), faces (16, 17), and visual words (18).

While these results in total support the functional specialization of visual cortex in humans, they also suggest significant differences between species in the location or function of some of these visual areas. For example, the location of putative V4 in humans in the ventromedial occipital cortex is at variance with its location on the lateral occipital surface in macaque monkey (1). Moreover, the same region or a nearby one is strongly activated by the presentation of visual words (18). Responses for face identity or gender in the human ventromedial occipital cortex (16, 17) are in contrast with the description of a high concentration of face selective cells in the superior temporal sulcus of macaque monkey (19). Although it is likely that some of these discrepancies will be solved by experiments more directly addressing analogies between visual areas in humans and monkeys, it is not inconceivable that different evolutionary pressures (e.g., language in humans) have induced significant anatomical or physiological differences, or both.

A second important issue raised by Dupont *et al.* (6) is the powerful influence of attention (and other cognitive processes) on visual processing. In their study, several additional visual areas were localized when the activity related to the stimulus itself (passive task) was subtracted from the activity related to the active processing of the same stimulus (detection, identification, or same trial discrimination).

It is well known that visual attention can modulate visual processing at the behavioral level and neuronal level. More recent is the notion that attentional modulations in a particular task (e.g., a motion, color, or orientation discrimination) are circumscribed to those areas that are preferentially tuned toward the incoming input. For example, Haenny *et al.* (20) and Spitzer *et al.* (21) have shown that attention to color and orientation modulate neuronal firing in area V4, which contains large amounts of chromatic bandwidth- and orientation-selective neurons. We have demonstrated with PET that directing attention to different features (e.g., color, motion, shape) of the same stimulus enhances blood flow responses in different regions of extrastriate cortex that are specialized for processing the selected attribute (9). In that experiment, attention was either focused on one attribute (selective attention) or divided among the attributes (divided attention) of a multidimensional visual display within a delayed matching-to-sample task. Similar effects have been found in the word visual area of the left lingual/fusiform gyrus during a semantic monitoring task that presumably directed attention to the word (22).

Blood-flow enhancement of specialized visual processors may therefore represent a common mechanism in extrastriate visual cortex for selecting the relevant feature of an object or relevant objects within a visual scene (perceptual grouping)—i.e., object-based attention.

In Dupont *et al.* (6) some of the visual responses might be explained by the attentional enhancement of orientation-related processors, but this is difficult to prove because attention was not explicitly manipulated. On the basis of their task analysis, Dupont *et al.* (6) interpret activity in the right area 19 from the subtraction STD − identification as mostly related to short-term memory and matching mechanisms. This is a remarkable result and is the first evidence for short-term memory mechanisms in human extrastriate visual cortex. Similar effects have been observed in macaque inferotemporal cortex (23, 24).

Orban *et al.* (7) have reported in a recent abstract activity from the same region during a concurrent discrimination task of spatial displacement and orientation. Concurrent discriminations concerned either the same object or different objects. The task did not involve sequential discrimination or short-term memory, and the activation is best explained as related to attentional or discriminatory mechanisms for orientation. Together these two experiments suggest that this region nearby area 19 handles orientation information across a variety of different tasks, and its activity can be modulated by both attentional, short-term memory, and matching signals.

In line with the idea that a visual area can perform multiple computation on incoming visual signals, Chelazzi *et al.* (25) have recently reported distinct neuronal signals in monkey inferotemporal (IT) cortex during a task in which animals were presented with a complex picture (the cue) to hold in memory and to be matched later with two to five choice pictures. IT cells showed different signals that were respectively correlated with the operation of encoding a cue, holding that cue on line in a delay period, and matching it to a stored template. Future experiments with PET or single-unit recording will have to distinguish between signals that are generated within an area from modulatory influences coming from other attentional areas.

Several other effects related to attention have been described with PET in the visual system. In contrast with the distributed nature of object-based attentional effects in extrastriate visual cortex, some regions in the superior parietal lobule (SPL) have been consistently driven by tasks that emphasize shifts of attention to different peripheral locations (space-based attention) (26). SPL is similarly activated: (*i*) when attention is driven by an external sensory change (e.g., a luminance transient in the peripheral visual field) or by an internal cognitive signal (e.g., spatial expectation) (*mode independence*); (*ii*) when the task involves either a manual key-press, an eye movement (27), or a covert response (*response independence*); (*iii*) during detection, discrimination, or imagery tasks (*task independence*). It has been proposed that this region implements a high-level operation for shifting the focus of processing at different map locations of external and internal space representations.

Conclusions

PET studies of vision and attention can contribute to the overall understanding of the visual system by providing information at the level of functional networks of cortical and subcortical areas. More progress will be made by carefully testing psychological and computational theories of vision and attention and by integrating neuroimaging techniques with electrophysiological methods. This will allow a more accurate temporal description of the pattern of activity propagating through such brain networks during mentation. The final goal of this approach is to map into the brain processing components or operations of behavior.

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